

PUBLIC CITIZEN HEALTH RESEARCH GROUP

Food and Drug Administration's Request for Comment on First Amendment Issues

Docket No. [02N-0209]

September 13, 2002

Public Citizen Health Research Group submits these comments in response to the vital public health concerns raised by the Food and Drug Administration (FDA) Notice dated May 16, 2002.

PUBLIC CITIZEN

Public Citizen is a national public interest organization, with over 125,000 members nationwide. Since its founding in 1971, Public Citizen has been active before Congress, regulatory agencies, and the courts in matters relating to public health in general and drug and medical device safety in particular. Through its Health Research Group, Public Citizen has submitted comments on FDA proposed rules relating to regulation of drugs, devices, and dietary supplements, and has petitioned the FDA to take action to remove unsafe products from the market.

The organization has also been in the vanguard in pressing for extending constitutional protection for truthful commercial speech. For example, Public Citizen's attorneys represented the consumer plaintiffs in *Virginia State Board of Pharmacy v. Virginia Citizens Consumer Council, Inc.*, the first case recognizing that commercial speech is entitled to significant protection under the first amendment.¹ Recently, we have also handled two other commercial speech cases.^{2, 3} We have also filed amicus briefs in a number of other commercial speech cases.^{4, 5, 6, 7}

Public Citizen Health Research Group submits these comments to highlight the interests of the people who have the most at stake in this matter – ordinary consumers.

INTRODUCTION

As the Supreme Court has repeatedly stated, misleading commercial speech may be regulated without running afoul of the First Amendment.^{8, 9}

In the area of food and drug law, health claims unsupported by significant and reputable scientific evidence are unreliable and misleading. Where the public health is threatened by such claims, they can be suppressed in their entirety. As the Supreme Court has emphasized:

Obviously, much commercial speech is not probably false, or even wholly false, but only deceptive or misleading. We foresee no obstacle to a State's dealing effectively with this problem. The First Amendment, as we construe it today, does not prohibit the State from insuring that the stream of commercial information flows cleanly as well as freely.¹⁰

As the Congress recognized in enacting the Food, Drug and Cosmetic Act, there are few if any absolutes in terms of safety of drugs and medical devices. Therapies well tolerated by many – even aspirin – pose a risk to some. Accordingly, the Act is premised on the idea that the FDA, in each instance, ought to weigh the potential benefits of drugs and devices against the risks that they carry. For that reason, the safety and effectiveness of drugs and medical devices is a relative thing and not a matter of absolute truths. Accordingly, the FDA is empowered to determine whether a new drug application is supported by “substantial evidence” or an application for premarket approval of a medical device offers “reasonable assurance” of safety and effectiveness of the product for specified indications.^{11, 12} Of course, even FDA approval is no guarantee of safety and effectiveness. Eight new drugs approved since the mid-1990s have subsequently been withdrawn from the market for safety reasons. Nonetheless, the FDA's review ensures an objective scientific evaluation of the relative safety of proposed products and the health claims that manufacturers want to employ to sell their products.

The FDA does not approve drugs and devices generally; it approves them for specific indications. For example, in November 2001, the FDA approved a new drug application for the drug valdecoxib (Bextra) for the treatment of the signs and symptoms of osteo - and rheumatoid arthritis and painful menses, but denied the New Drug Application insofar as it sought approval to market the product to treat acute pain. In other words, the FDA found insufficient assurance that the drug was safe and effective for the latter use. The marketers of this drug, Pfizer and Pharmacia, later issued a press release announcing the publication of a study – sponsored by the companies – that concluded that valdecoxib was effective in treating acute pain. The issue addressed in these comments is whether publication of a study in those circumstances constitutes misleading commercial speech, or whether, despite the FDA's rejection of approval for this indication, the companies were entitled to make this claim under the First Amendment.

DISCUSSION

The concept of “truth” in the realm of science is an elusive one. According to the dictionary, the word truth means “the state of being the case: fact.” But in science facts are hard to come by and then open to question. Galileo's conception of the universe might have been accepted as “fact” until Copernicus demonstrated the error in Galileo's theory. And in trying to ascertain the facts about the relative risks and benefits of drugs and medical devices, the “truth” is often uncertain, even when the best scientific

methods are used for evaluation. Sellers can take advantage of uncertainty by making claims that are not certain to be true, but are not yet demonstrably or certainly false. Government can serve no more important role than to level the information playing field about drugs and medical devices for patients. This is a function that has not been effectively filled by the FDA, and the FDA's ability to do so has now been called into question by this request for comment.

Government must play an active role in proctoring the information drug and medical device manufacturers provide to physicians and patients because the incentives for the manufacturers to distort the "truth" by providing the public a misleading, one-sided presentation of the scientific evidence, are enormous. These manufacturers operate in highly competitive environments and owe a fiduciary duty to their stockholders to maximize the profits and growth of the company as best as possible within the bounds of the law. So it is no surprise that their promotional material accentuates the positives of their products and minimizes the risks.

While the Health Research Group is interested in all forms of communication between drug and device manufacturers and physicians and patients, these comments will focus on what we see as the breeding ground for the most egregious and worrisome abuses: "peer reviewed" literature circulated to physicians by drug companies.

We recognize that published research sponsored and controlled by a manufacturer about one of its drug products can be either pure scientific communication or a commercial message intended to influence the drug selection process. If companies were operating solely under the axiom that the research they sponsor and control will be published to further scientific knowledge, in the interest of public welfare, then all research sponsored and controlled by a company would be freely published, both that which reflects positively and negatively on a particular drug. But that is not how drug and device companies work. Most publish favorable results, but are wary of, and often decline to, publish negative results. But plainly a decision to publish negative results when, for example, positive results have already appeared in the literature, when it is clear that the publication of the positive results, untempered by subsequent negative findings, is plainly a promotional communication, and little else.

Compounding the negative effects on the public health of published research that appears to be a scientific communication that may, in fact, be a misleading promotion is that such a misleading promotional publication is almost always undetectable by the commercial audience.

One of the keys to the definition of what constitutes truthful speech regarding a pharmaceutical is an appreciation of the meaning of truth, by necessity, in the scientific sense. As we said above, scientific truth is a "moving target" and there is always a level

of uncertainty that is implicit in the definition of scientific truth.

The legal standard for marketing a new drug in the United States is not proof that the drug is effective, as an indisputable fact, but rather that there is substantial evidence of the drug's efficacy. Substantial evidence is defined as:

...evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.¹³

The standard is a procedure, not a definition, established by Congress to create a standard of evidence that provides the public a level of certainty, not absolute certainty, that a "... drug will have the effect it purports or is represented to have" Congress delegated the responsibility for determining substantial evidence to the FDA.

The quality of evidence used by the FDA in making a determination to approve a new drug, or to approve an old drug for a new use, is significantly greater than that found in a peer reviewed medical journal study. A single peer reviewed medical journal article may be the sole foundation for prescribing a drug for an off-label use. The agency bases its determination of efficacy on its own examination of the data, including statistical analyses done by highly skilled, Ph.D.- level statisticians. In addition, the FDA has the authority and the responsibility to audit clinical research sites to ensure that the data the agency uses in making its decisions are valid.

The FDA's method contrasts sharply with the process that medical journal editors use in deciding whether or not to publish a study. Medical journal editors accept the veracity of a manuscript submitted for publication. The journal editor has neither the authority nor the resources to audit clinical research sites. The journal editor may reject the manuscript outright as poor science or send the manuscript for peer review, a process that may take as little as a few hours of the reviewer's time. If the author of a manuscript persists, no matter the quality of the work, the manuscript will almost invariably be published in a peer reviewed journal.

One example of the substantial disparity between the FDA's approval process and the published medical literature are surveys demonstrating statistical errors in a large percentage of studies appearing in medical journals over the past 25 years.^{14, 15, 16, 17, 18, 19, 20} If an incorrect statistical test is chosen by the author(s) of a peer reviewed medical journal article in arriving at a conclusion, the conclusion is invalid.

The arguments proposed by those who contend that the First Amendment forbids restrictions on the distribution of peer reviewed medical journals for promotional purpose are premised on the idea – wholly inaccurate in our view – that practicing physicians because of their medical expertise can distinguish between peer review journals of sound quality and those that employ faulty statistical methodology. But the evidence suggests that the statistical mistakes that are far too common in peer review journals escape the attention not just of the journal's editors, but of all but the most sophisticated readers. Put simply, physicians are at risk of accepting uncritically the published results in a peer review journal as are the editors of such journals.

This concern is strengthened by the fact that a number of studies have documented the lack of understanding by many physicians of basic statistical concepts. The available evidence suggests that most physicians depend on the journals, through the editorial and peer review processes, to ensure that the statistical methods in published research are being used and interpreted properly. Except in the largest circulation medical journals, the probability of statistical methodologic review of original research is low.²¹

In the 1962 Kefauver-Harris amendments to the Food, Drug and Cosmetic Act that established an efficacy requirement for the marketing of new drugs, Congress made the judgment that physicians are not qualified to choose drugs for their patients without the help of experts (the FDA) in weeding out ineffective drugs and leaving only drugs whose efficacy has been proven on the market. Congress also recognized that the market could not weed out worthless or dangerous drugs, misleadingly promoted for unsubstantiated uses. Markets do fail, particularly those that are characterized by imperfect information, such as the pharmaceutical marketplace.

The FDA's approval process does not eliminate uncertainty about the safety and efficacy of a new drug. However, to suggest that the conclusion of a peer reviewed medical journal article is comparable to the FDA's drug approval process is untenable. On what logical basis can it possibly be argued that the initial FDA approved claim for a drug, say the relief of pain, should be supported by the standard of substantial evidence, but that successive claims, for instance the cure of acne reported in a medical journal, need not be so supported?

The remainder of these comments consist of four examples that illustrate that patients have been and are now being harmed both physically and economically from the promotion of drugs for off-label uses.

The first example is the antibiotic chloramphenicol (Chloromycetin), a drug that is now over 50 years old. Promotion for unsubstantiated uses led to its indiscriminate use and patients needlessly died from a blood disorder.

Valdecoxib (Bextra), a redundant nonsteroidal anti-inflammatory drug (NSAID), is the second example. This drug was promoted off-label for acute pain using the peer reviewed medical literature. The FDA was complicit in this promotion by not releasing to the public information about the failure of valdecoxib to gain approval for the treatment of acute pain. This also may be viewed as promotion of valdecoxib for a disapproved use.

The last two examples involve the tremendously popular drugs, celecoxib (Celebrex) and gabapentin (Neurontin). Together, more than 27 million prescriptions were written for these drugs with total sales exceeding \$ 3.7 billion in 2001. In both cases, misleading promotional peer reviewed medical literature articles were used to stimulate sales, to the detriment of the public.

Little has changed since Congress prohibited the promotion of prescription drugs for uses other than those approved by the FDA, with the possible exception of the sophistication of promotional strategies now being used by the pharmaceutical industry.

CHLORAMPHENICOL (CHLOROMYCETIN)²²

One of the earliest and most carefully documented cases of the negative effect of drug promotion on the public health and safety concerns the antibiotic chloramphenicol (Chloromycetin), a drug first marketed in 1949 by Parke Davis. Chloramphenicol had a legitimate role in the treatment of serious and potentially fatal infections and today is reserved only for severe infections when less hazardous drugs are ineffective.

The first warning linking chloramphenicol to a serious blood disorder appeared in 1949 at the time of its initial marketing. By 1952 it had become clear that chloramphenicol could cause aplastic anemia, a potentially fatal adverse reaction, and other blood disorders. A strong warning of possible blood damage was published in 1953. At this time, the FDA, in conjunction with the National Research Council, documented the link between chloramphenicol and blood damage. The FDA ordered warnings added to the drug's professional product information and made a recommendation that chloramphenicol not be used indiscriminately or for trivial infections. The warnings caused a precipitous fall in chloramphenicol sales, but only temporarily. Parke-Davis intensified its promotion of the drug and sales again soared.

In 1960, the *Journal of the American Medical Association* wrote:

Although the warning statement specifically cautions against the indiscriminate use of the drug or against its use for minor infection, an examination of the reports received by the registry reveals that the drug has been used in such conditions as upper respiratory infections, including the common cold, bronchial

infections, asthma, sore throat, and tonsillitis, miscellaneous urinary tract and ear infections, undiagnosed low-grade fever, and even disseminated lupus erythematosus, gout, eczema, malaise, and iron deficiency anemia.

Sales of chloramphenicol were off markedly in 1961, but the downturn was short-lived, and by 1962 a reversal in production of the drug and number of prescriptions had begun. Surveys indicated that perhaps 90 percent of the patients treated with chloramphenicol received it for inappropriate reasons that raises serious questions about the "expertise" of physicians.

In November 1967, Senator Gaylord Nelson (D-WI) held hearings about antibiotics in general and chloramphenicol in particular. The publicity engendered by these hearings finally led the public and the medical profession to appreciate the dangers of chloramphenicol. By 1968 chloramphenicol prescribing was plunging precipitously.

Senator Nelson caustically remarked to a spokesperson for the American Medical Association defending the prescribing practices of American physicians during the hearings "... many doctors have been blind, dumb, and deaf. It has been a horrible tragedy in this country and it is an indictment of the medical profession."

Free market proponents are fond of insisting that companies will not engage in the misleading promotion of their products and will act in enlightened self interest not to sully their reputations that could negatively affect sales. A dip in sales is easily corrected by only increasing advertising. Parke-Davis and chloramphenicol is only a first example of this type of behavior. Any suggestion that the health and safety of the American public should be left to the whims of the marketplace is irresponsible.

VALDECOXIB (BEXTRA)

A more recent example of a peer reviewed journal article that is inherently misleading involves the drug valdecoxib (Bextra), a nonsteroidal anti-inflammatory drug (NSAID) marketed by Pfizer and Pharmacia that was approved on November 16, 2001. Approval of valdecoxib brought to over 20 the number of drugs in this class. A press release six months earlier indicated that approval for the treatment of acute pain was being sought for valdecoxib.²³ But valdecoxib did not receive FDA approval for acute pain.²⁴ The Health Research Group examined the FDA reviews for valdecoxib posted on the agency's Web site and found that all information concerning the efficacy of the drug for the treatment of acute pain had been removed from the reviews. We were told that it is FDA policy to remove information about a use for a new drug that failed to be approved. The agency's explanation was that this information is exempt from Freedom of Information Act (FOIA) disclosure because it is confidential commercial information.

Yet, at the same time the Health Research Group was attempting to access information about the use of valdecoxib and acute pain, a press release²⁵ was issued announcing the publication of studies in the *Journal of the American Dental Association (JADA)*²⁶ that claimed effectiveness for valdecoxib in the treatment of acute pain associated with dental surgery.

This publication was co-sponsored by Pfizer and Pharmacia. Three of the five authors were employees of Pharmacia, the corporation's director of Biostatistics, director of Medical Development, and the clinical vice-president of Medical Development. These three individuals certainly must have known that valdecoxib failed to gain FDA approval for acute pain.

Again, only those studies showing valdecoxib in the brightest light appeared in the medical literature at the time – preceded by a press release. Pfizer and Pharmacia cannot claim that they followed the scientific standard of communication with their JADA publication and at the same time claim that negative studies are confidential commercial information when they announced that they were seeking approval for the treatment of acute pain for valdecoxib from the FDA. The JADA publication can only be considered to be misleading promotion on the part of these companies.

Valdecoxib is also an example where agency FOIA policy has kept physicians in the dark that has contributed to the misleading promotion of the drug. Present FDA policy tips the information playing field totally in favor of the sellers (the pharmaceutical industry) allowing them to selectively communicate only the positive aspects of their products, while using FOIA to claim that negative evidence is confidential commercial information. This can cause patients to purchase drugs that may be less safe and less effective, or both, at exorbitant prices.

CELECOXIB (CELEBREX)

Celecoxib, a drug marketed by Pfizer and Pharmacia, exploded onto the market in early 1999 with a successfully managed media campaign calling it "super-aspirin"– a "breakthrough" drug that is as effective as the older NSAIDs and supposedly without the same risk of gastrointestinal (GI) toxicity, the adverse effect that is the most serious concern with the use of NSAIDs.

Overlooked by uncritical journalists, too many physicians and a duped public was the fact that celecoxib was approved by the FDA with exactly the same warnings about risk of GI bleeding and death as the other 19 NSAIDs that were on the market at that time. Celecoxib's manufacturer could not, and has not, proved to the FDA that their drug was any safer as far as GI toxicity is concerned, than the legion of other NSAIDs already available at much lower cost.

Celecoxib is remarkable in one respect. Despite the fact that it is an unremarkable treatment for arthritis and pain, it racked up \$1 billion in sales before a single clinical trial was published comparing it to an existing drug for the treatment of arthritis.²⁷ In recent years, the core business of the pharmaceutical industry has been marketing, not research, and celecoxib is the icon of how successful marketing can be, even for a drug that is no better or safer (just more expensive) than drugs already on the market.

Pfizer and Pharmacia scored an apparent advertising coup with the publication of the CLASS study (Celecoxib Long-term Arthritis Safety Study) in the September 13, 2000 issue of the *Journal of the American Medical Association (JAMA)*.²⁸ The results of this six-month-long study were "spun" to conclude that celecoxib was safer on the GI tract than other NSAIDs. A cautiously optimistic editorial about the therapeutic benefits of celecoxib accompanied the publication of the CLASS study.²⁹

The FDA's Arthritis Advisory Committee met on February 7, 2001, to review a request to change celecoxib's labeling to indicate that it is a GI-safe NSAID, based on the results of the CLASS study. At this meeting it was revealed that the company actually had data on the safety of celecoxib for as long as 16 months rather than just the six months of results published in the *JAMA*.

The FDA medical officer who reviewed the CLASS study for the February advisory committee meeting concluded that the company had failed to show a statistically significant lower rate of serious GI adverse reactions compared to usual doses of the NSAIDs ibuprofen (Motrin) and diclofenac (Voltaren).³⁰

The misleading findings published in the original *JAMA* article appear to be widely distributed and believed. Approximately 30,000 reprints of the CLASS study were bought from the publisher and a recent search of the Science Citation Index yielded 169 other articles citing CLASS within months of its publication. This wide distribution and citation has coincided with the sales of celecoxib increasing from \$2.62 billion in 2000 to \$3.1 billion in 2001.³¹

The FDA has indicated that it is investigating whether the company knowingly disseminated the misleading CLASS reprints.³²

GABAPENTIN (NEURONTIN)

This drug was originally produced by Parke-Davis, which was acquired by Pfizer, Inc, of New York in 2000. The only FDA approved use for gabapentin at that time was as an add-on treatment for epilepsy. This is a very limited market with little upward sales potential. Court documents in a civil case recently unsealed from the United States District Court in Massachusetts allege that Parke-Davis knew that pain

management, psychiatric disorders, anxiety and depression, all off-label uses, were immense markets which, if tapped, could yield enormous profits from sales of gabapentin. The company made a measured economic decision to make an "end-run" around the FDA's drug approval process and promote gabapentin for unsubstantiated uses.

According to the court documents, after an extensive economic analysis, senior officials at Parke-Davis determined that it was not sufficiently profitable for Parke-Davis to obtain FDA approval for gabapentin's alternative uses by doing the types of studies necessary for approval. Instead, company officials developed a strategy that would allow Parke-Davis to avoid the costs of proving gabapentin's safety and effectiveness for these other uses, while allowing the company to enter the lucrative off-label markets.

Taking advantage of a loophole in the FDA's off-label marketing rules, Parke-Davis decided to employ a "publication strategy" that would allow it to promote gabapentin by the massive distribution of publications supposedly written by independent researchers who purportedly described the scientific evaluation of gabapentin. Another advantage of this strategy, from the company's perspective, was that it could be done immediately. There was no need to wait for the results of scientifically conducted clinical trials to determine if gabapentin was actually effective in the treatment of these conditions and submit them to the FDA for approval.

The company's "publication strategy" required physicians to perform the work normally performed by the company's sales force. This necessitated that Parke-Davis make tens of thousands of payments to the physicians who would act as a surrogate sales force as well as to the practicing physicians who would receive the message. In other words, adoption of the "publication strategy" required the company to pay physicians to either recommend the prescription of gabapentin or to order gabapentin, in violation of the federal anti-kickback regulations, according to allegations made in court documents.

A common tactic used by Parke-Davis to funnel payments to physicians to encourage them to prescribe gabapentin off-label was through "consultants" meetings. Under this front, Parke-Davis invited doctors to dinners or conferences and paid them to hear presentations about off-label uses of the drug. Under the guise that these physicians were acting as consultants, Parke-Davis sometimes, but not always, had the physicians sign bogus consulting agreements. At these meetings, the company would give these physicians lengthy presentations relating to gabapentin, particularly regarding off-label usage. Presentations would be made by Parke-Davis employees or physician speakers hired by the company for the purpose of promoting gabapentin, and questions relating to the use of gabapentin would be solicited and answered. At some conferences, the sponsoring organization or Parke-Davis intentionally posed questions to the speakers about off-label use to insure that the physicians were exposed to such information.

Parke-Davis would routinely analyze whether the consultants' meetings were successful in getting physicians to change their prescription writing practices. At some meetings, the so-called consultants were asked directly if they would write more gabapentin prescriptions as a result of the meeting. This question would have been irrelevant if the actual purpose of the meeting was to receive the consultants' advice. Parke-Davis also routinely tracked consultants' gabapentin prescription writing practices after these meetings. Parke-Davis actually analyzed whether the doctors they had paid had in fact written more gabapentin prescriptions after the meeting, using market data purchased from third parties.

The court documents revealed another platform used by the company to pay kickbacks to physicians to hear off-label promotion of gabapentin. These were programs billed as Continuing Medical Education (CME) seminars. These conferences and seminars were set up to appear to qualify for an exception to the FDA's off-label marketing restrictions which permits doctors to learn about off-label uses of drugs at independent seminars. Such seminars, however, must be truly independent of the drug companies. The companies may make "unrestricted grants" for the purpose of a seminar, but may not be involved in formulating the content of the presentations, picking the speakers or selecting who attends the seminars. Parke-Davis retained third party companies to present seminars while in fact retaining control of virtually every aspect of these events. The seminar companies obtained Parke-Davis' approval for all content presented at the seminars. Parke-Davis also paid all expenses, including all the seminar companies' fees.

The company designed and approved the seminars, hand-picked the speakers, approved the seminar presentations, previewed (in most cases) the contents of the seminars prior to a presentation, selected the attendees based on their ability and willingness to prescribe high quantities of gabapentin, evaluated the presentations to make sure Parke-Davis' "message" was appropriately delivered, black-listed presenters whose presentations were not sufficiently pro-gabapentin, and monitored the prescribing patterns of the physicians who attended.

Parke-Davis also made outright payments, in the form of grants, to reward demonstrated gabapentin advocates. Company sales managers identified key physicians who actively prescribed gabapentin or programs which were willing to host gabapentin speakers and encouraged such persons or programs to obtain "educational grants" from the company. Parke-Davis' sales people informed leading gabapentin subscribers that significant advocacy for gabapentin would result in the payment of large grants.

Another method of paying physicians for backing gabapentin was to pay honoraria for the use of their names on scientific articles intended for publication in various neurology and psychiatry journals. These articles were allegedly ghost-written by technical writers hired by Parke-Davis, which retained control of all such articles. In 1996 Parke-Davis paid for at least 20 such articles, most of which dealt with off-label

use of gabapentin, and were placed according to the company's "publication strategy."

Once Parke-Davis and the technical writers conceived the articles, the company and its outside firms attempted to find recognized gabapentin prescribers whose names could be used as the authors of these articles. In some cases, drafts of the articles were completed even before an "author" agreed to place his or her name on the article. This even occurred in connection with case histories that purported to describe the "authors" personal treatment of actual patients. The "authors" were paid an honorarium of \$1,000.00 to lend their names to these articles, and also were able to claim publication credit on their professional resumes.

According to the court documents, Parke-Davis also formed a Speakers' Bureau, another tactic to make large and numerous payments to physicians who recommended gabapentin at teleconferences, dinner meetings, consultants meetings, educational seminars, and other events. These speakers repeatedly gave short presentations relating to gabapentin for which they were paid anywhere from \$250 to \$3,000. Some speakers received tens of thousands of dollars annually in exchange for recommending to fellow physicians that gabapentin be prescribed, particularly for off-label uses. Speakers who most zealously advocated gabapentin were hired most frequently for speaking events, regardless of the fact that many of these events were billed as independent medical education seminars where objective information was supposed to be delivered.

The revelations surrounding the success of gabapentin have shattered some widely held myths.

First, and perhaps most important to the health and safety of patients, is the belief that physicians are not fooled or influenced by drug company promotional ploys such as gifts to attend medical meetings or expensive meals. The evidence presented in the court documents unambiguously shows that such schemes work and underscores why Congress created a process by which the FDA approves drugs based on validated science for specific uses – to protect the public.

Second, the sacrosanct position of peer reviewed medical literature as a vehicle for scientific exchange has been seriously damaged. In defense of the many physicians who do try their best for patients by diligently keeping up with the medical literature, there is no way for a physician, scientist, or medical journal editor to know if a published study is a part of a carefully orchestrated promotional strategy by a company or science.

Circumstantial and some direct evidence over the years suggests that the behavior of Parke-Davis in the off-label promotion of gabapentin is not isolated, but rather an integral part of the pharmaceutical industry's marketing practices. In our experience, the gabapentin episode is the most complete and well documented case of off-label promotion to ever come into public view. Because of the detail of fabrications,

pay-offs, manipulation, and their effect on gabapentin sales the Amended Complaint in this case is presented as Attachment I to these comments.

CONCLUSIONS

The decision by Congress over four decades ago to limit the promotion of pharmaceuticals to their FDA approved uses was carefully considered and based on evidence that patients were being harmed, both physically and financially, from products promoted for uses for which they had not met the legal standard for safety and effectiveness. Patient protection from the off-label promotion of drugs was seriously undermined with the passage of the 1997 Food and Drug Administration Modernization Act. And because there are no adequate systems in place in the general population to determine who is harmed from drugs, let alone if anyone is helped, there is no reason to believe that patients today are at less risk of physical or financial harm than they were four decades ago from the off-label promotion of drugs.

The extent to which the pharmaceutical industry controls the flow of information about its products is chilling, including the opportunity to manipulate the peer reviewed medical literature. The notion that market forces or physician expertise can adequately protect the public from being prescribed drugs for uses for which they have not been shown to be safe and effective flies in the face of the facts.

To the extent that the FDA has authority under the law to regulate prescription drug promotion, including off-label promotion, the agency should err on the side of public protection and not pander to the commercial interests of the pharmaceutical industry.



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30. Goldkind L. Medical Officer's Gastroenterology Advisory Committee Briefing Document, June 12, 2000, p.68.
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ATTACHMENT I

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

)	Civil Action No. 96-11651--PBS
)	
UNITED STATES OF AMERICA)	
ex rel. DAVID FRANKLIN,)	
Plaintiff,)	
)	<u>AMENDED COMPLAINT</u>
v.)	(Filed Under Seal)
)	
PFIZER, INC., and PARKE-DAVIS,)	
DIVISION OF WARNER-LAMBERT)	
COMPANY)	
Defendant)	
)	

I. PARTIES

1. Relator David Franklin is a resident of the Commonwealth of Massachusetts and a former employee of the Parke-Davis division of Warner-Lambert Company ("Parke-Davis"). David Franklin is the original source of the facts and information hereinafter set forth concerning the activities of Parke-Davis. The facts averred herein are based upon his personal observation, documents in his possession, and documents produced in discovery in this action.

2. Defendant Pfizer, Inc. ("Pfizer") is a Delaware corporation with a principal place of business in New York, New York. Pfizer is principally engaged in the manufacture and sale of pharmaceuticals. In 2000, Pfizer acquired Warner-Lambert Company (Warner-Lambert) including Warner-Lambert's Parke-Davis division ("Parke-Davis"). As a result of the acquisition, Pfizer is responsible for all liabilities which result from any acts or omissions of Parke-Davis or Warner-Lambert which occurred prior to the Warner-Lambert acquisition.

3. Parke-Davis was, until 2000, a division of Warner-Lambert, a corporation with a principal place of business in Morris Plains, New Jersey. At all times material hereto Parke-Davis was principally engaged in the sale and manufacture of pharmaceuticals including prescription pharmaceuticals falling under the jurisdiction and regulation of the United States Food and Drug Administration (FDA).

II. JURISDICTION

4. Jurisdiction is based on 31 U.S.C. §3730 and 28 U.S.C. § 1331.

5. At all times material hereto, Parke-Davis and/or Pfizer regularly conducted substantial business within the Commonwealth of Massachusetts, maintained permanent employees and offices in Massachusetts and made and is making significant sales within Massachusetts. Accordingly, Pfizer is subject to personal jurisdiction in the Commonwealth of Massachusetts pursuant to M.G.L.c. 223A §3.

6. Venue is appropriate in the District of Massachusetts pursuant to 28 U.S.C. §1391(b)(1) and (2).

III. FACTS

7. More prescription drugs are purchased through the Medicaid program than through any other insurance program in the United States. The federal government provides most of the funds used to purchase these pharmaceuticals. Not surprisingly, in order to prevent waste, fraud and abuse, the Medicaid program restricts the types and uses of drugs which may be paid for with federal funds. Additionally, federal regulations prohibit certain marketing practices which have a propensity to lead to the unnecessary and ineffective prescription of pharmaceuticals. These regulatory schemes are designed to insure that Medicaid only pays for drugs which are found to be safe and effective for

their prescribed uses, and to insure that physicians who prescribe such drugs do not have ulterior motives for prescribing drugs that will be purchased with federal funds.

8. In this *qui tam* action Relator David Franklin alleges that Parke-Davis knowingly and deliberately engaged in conduct it knew would lead to the violations of federal Medicaid statutes and regulations designed to restrict Medicaid reimbursement for one of Parke-Davis' patented drugs, Neurontin. Parke-Davis did not directly provide Neurontin to the Medicaid program or issue prescriptions for the drug. Instead, Parke-Davis embarked on a course of unlawful conduct that it knew would lead to the submission by physicians and pharmacists of thousands of Medicaid claims for Neurontin when such prescriptions were not eligible for Medicaid reimbursement. Although most of the physicians and pharmacists were unaware that their Medicaid claims were ineligible for reimbursement, Parke-Davis knew its actions would inevitably cause these Medicaid providers to submit false claims to the federal government. Relator, in the name of the United States, seeks to hold Parke-Davis liable for knowingly causing these false claims to be presented to the United States for payment in violation of 31 U.S.C. § 3729.

A. The Regulatory Scheme That Restricts the Marketing and Reimbursement of Neurontin

9. New pharmaceutical drugs may not be marketed in the United States until the sponsor of the pharmaceutical has proven to the Food and Drug Administration (FDA) that the drug is safe and effective for specific indications at specified dosages. The indications and dosages approved by the FDA are set forth in the drug's labeling, the content of which is also approved by the FDA. Although it is not unlawful for physicians to prescribe approved drugs for indications or at dosages different than those set forth in a drug's labeling, The Food Drug and Cosmetic Act prohibits drug

companies from marketing or promoting approved drugs for uses other than those set forth in the drugs' approved labeling. This regulatory scheme protects patients and consumers by insuring that drug companies do not promote drugs for uses other than those found to be safe and effective by an independent, scientific governmental body.

10. The Medicaid program also relies on the FDA's findings regarding what uses for approved drugs are safe and effective. In 1990, Congress passed the Budget Reconciliation Act which limited reimbursement for prescription drugs to "covered outpatient drugs." Covered outpatient drugs only include drugs used for "medically accepted indications." A medically accepted indication is a use which has been approved by the FDA or one which is supported by specific compendia set forth in the Medicaid statute. Until August, 1997 none of the compendia referenced in the statute supported off-label usage of any approved drugs. Even after August 1997, off-label usage was significantly restricted.

11. The Medicare and Medicaid anti-kickback laws, 42 U.S.C. § 1320a-7b(b) also regulate drug marketing in order to prevent overutilization of prescription medication. Under the anti-kickback laws, drug companies may not offer or pay any remuneration, in cash or kind, to induce physicians or others to order or recommend drugs which may be paid for by a federal healthcare program such as Medicare or Medicaid. These regulations not only prohibit outright bribes and rebate schemes, but prohibit any payment by a drug company to a physician which has as one of its purposes the inducing of the physician to write additional prescriptions for the company's pharmaceuticals.

12. Concern about improper drug marketing practices increased at just about the time Parke-Davis began its marketing of Neurontin. In 1994 the Inspector General of the Department of

Health and Human Services issued a Special Fraud Alert concerning prescription drug marketing practices that violated the anti-kickback laws. Among the improper practices cited by the Inspector General were drug companies' payment of "research grants" to substantial prescribers of its medications; payments to physicians for "studies" of the company's products when the studies were "of questionable scientific value and require little or no actual scientific pursuit"; and payments to physicians where the physician had offered no particular services of benefit to the drug company but the payment appeared to have been based on the volume of business the doctor generated in the past, or could generate in the future, for the drug company.

13. As described below, Parke-Davis between 1994 through at least 1998, and probably thereafter, knowingly and intentionally violated the regulatory schemes described above in their marketing of Neurontin. When it intentionally decided to employ these improper marketing practices to promote Neurontin, Parke-Davis knew or should have known that pharmacists and physicians would routinely and necessarily file false claims with the federal government when they sought federal reimbursement for Neurontin prescriptions. But for Parke-Davis' actions most, if not all, of the false claims for the prescription of Neurontin would never have been filed. Although it did not directly contract with the federal government, Parke-Davis was the indirect beneficiary of all of the false claims described herein.

B. Parke-Davis' Deliberate Decision to Avoid FDA Approval and Market Neurontin Off-Label.

14. In December 1993, the FDA approved Neurontin as "adjunctive therapy" for the treatment of certain types of these seizures in adult patients suffering from epilepsy. "Adjunctive therapy" meant that the drug could not be prescribed by itself for the treatment of epilepsy, but as

an add-on drug in the event that a primary anti-epilepsy drug was not successful. The FDA approved labeling of Neurontin stated that the drug is only effective at 900 to 1800 mg/day.

15. At the time Neurontin was approved, Parke-Davis' original patent on Neurontin was set to expire in December 1998. This left Parke-Davis with only a small window of exclusivity for this drug; after the expiration of the Neurontin patent Parke-Davis would be forced to share the market for Neurontin with generic drug manufacturers, substantially reducing its profits and its ability to keep Neurontin's retail price high.

16. At the time Parke-Davis filed its NDA (New Drug Application) with the FDA Parke-Davis intended Neurontin to be used for other indications besides epilepsy adjunctive therapy. In October 1990, Parke-Davis filed a patent for Neurontin claiming it to be effective in the treatment of depression. In November 1990, it filed another patent application for Neurontin claiming it to be effective for the treatment of neurodegenerative disease. In 1995, prior to the Relator becoming an employee of Parke-Davis, additional patent applications were filed by Parke-Davis for mania and bipolar disease and for anxiety and panic. Notwithstanding the claims made in its patent applications, neither Parke-Davis nor Pfizer ever sought FDA approval for the use of Neurontin to treat the conditions described in the four patent applications referenced above.

17. The market for the only approved use for Neurontin, adjunctive therapy for epilepsy patients, is, and was, limited. On the other hand, the market for the other uses of Neurontin contemplated by Parke-Davis—pain management, psychiatric disorders, anxiety and depression—were huge. Parke-Davis knew that if these markets could be tapped, Parke-Davis could enjoy enormous profits from Neurontin.

18. Initially, Parke-Davis intended to file supplemental NDAs in order to expand Neurontin's approved indications, including applications for monotherapy (which would permit Neurontin to be prescribed by itself for epilepsy treatment) and for various psychiatric and neurological indications. However, by 1995 Parke-Davis recognized it would be uneconomical to assume the expense and time necessary to conduct clinical trials necessary to prove that Neurontin was safe and effective for these uses. Assuming Neurontin could be proven to be safe and effective, the near term expiration of the patent meant that generic manufacturers of Neurontin would reap much of the reward of proving Neurontin could be safely used for other indications.

19. After performing extensive economic analysis, senior officials at Parke-Davis determined that it was not sufficiently profitable for Parke-Davis to obtain FDA approval for Neurontin's alternative uses. Instead, Parke-Davis officials developed a strategy that would allow Parke-Davis to avoid the costs of proving that Neurontin was safe and effective for these other uses, while allowing Parke-Davis to compete in the lucrative off-label markets. Taking advantage of a loophole in the FDA's off-label marketing rules, Parke-Davis decided to employ a "publication strategy" that would allow it to promote Neurontin by the massive distribution of publications supposedly written by independent researchers that purportedly described the scientific evaluation of Neurontin. Another advantage of this strategy, from Parke-Davis' perspective, was that it could be employed immediately—there was no need to wait for the results of scientifically conducted clinical trials to determine if Neurontin was actually effective in the treatment of these conditions.

20. Although federal regulations did not permit Parke-Davis to promote unapproved uses of Neurontin, Parke-Davis was permitted to distribute publications created by third parties that described results of off-labeled use of Neurontin, provided such material was only distributed in

response to non-solicited requests from physicians. Parke-Davis decided to exploit this narrow exception by creating events and programs that would allow special Parke-Davis employees and independent contractors under Parke-Davis' control to promote off-label usage under circumstances that would allow the company to plausibly deny that it had solicited off-label usage.

21. Significant ingenuity and resourcefulness was necessary in order to execute this unlawful scheme without detection. Faced with the fact that its "publication strategy" required publications from independent physicians when no such publications existed, Parke-Davis hired non-physician technical writers to create articles for medical journals and then paid actual specialists to be the articles' "authors". Faced with the fact that its normal marketing force could not deliver the off label message, Parke-Davis trained its medical liaisons, technical employees who were supposed to provide balanced scientific information to doctors, to sell off-label and solicit interest in off label uses. And faced with the fact that in order for a "publication strategy" to actually increase usage of a drug, Parke-Davis required a large group of doctors interested in experimenting on patients, and an even larger group of doctors who were interested in receiving information about those experiments. Parke-Davis generated both groups by liberally distributing payments to both groups of physicians through "consultants" meetings, speakers bureaus, medical education seminars, grants, "studies", advisory boards and teleconferences. Further details of these programs are described below.

22. Notwithstanding their knowledge that they could not promote Neurontin lawfully for non-approved uses, marketing executives at Parke-Davis' headquarters in Morris Plains, New Jersey and in its five regional customer business units (CBUs) selected a marketing strategy which would deliberately lead to increased off-label usage of Neurontin. These executives knew that Parke-Davis

was not supposed to create or design the contents of the communications that would be distributed pursuant to the “publication strategy” or do anything to generate the practicing physicians’ interest in receiving such communications. As demonstrated below, Parke-Davis ignored these legal requirements and, instead, put into effect a pervasive pattern of illegal conduct, described below, lasting from at least 1994 through 1998, and Plaintiff believes, through 2000.

C. Parke-Davis’ Systematic Payments to Doctors for the Purpose of Increasing Neurontin Prescriptions

23. Parke-Davis’ “publication strategy” required physicians (and its medical liaisons) to perform the work normally performed by the Company’s salesman in order to promote Neurontin. Adoption of this strategy required Parke-Davis to make tens of thousands of payments to the physicians who would act as a surrogate sales force as well as the practicing physicians who would receive the message. In other words, adoption of the “publication strategy” required Parke-Davis to make thousands of payments to physicians for the purpose of having those doctors either recommend the prescription of Neurontin or to order Neurontin, in violation of the Medicaid kickback regulations. Parke-Davis was aware that these regulations were violated routinely. A description of the various programs Parke-Davis used to make these payments to physicians follows.

Consultants’ Meetings

24. A common ploy by Parke-Davis to funnel illegal payments to physicians to encourage them to prescribe off-label was through “consultants” meetings. Under this guise Parke-Davis recruited physicians to dinners or conferences and paid them to hear presentations about off-label uses of Neurontin. Under the fiction that these doctors were acting as consultants, Parke-Davis sometimes (but not always) had the doctors sign sham consulting agreements. At these meetings

Parke-Davis would give these doctors lengthy presentations relating to Neurontin, particularly regarding off-label usage. Presentations would be made by Parke-Davis employees or physician speakers hired by Parke-Davis for the purpose of promoting Neurontin, and attendees' questions relating to the administration of Neurontin use would be solicited and answered. At some conferences, the sponsoring organization or Parke-Davis intentionally posed questions to the speakers about off-label use to insure that the attendees were exposed to such information.

25. At some, but not all, "consultants" meetings a few questions would be posed to the "consultants" regarding Parke-Davis marketing of Neurontin or how Parke-Davis sales force could provide better service to the doctors. The consultants' meetings, however, were not held (and the "consultants" were not paid) for the purpose of providing Parke-Davis with expert, independent advice. Parke-Davis in many cases did not even record the "advice" provided by its "consultants" and what advice was collected was never acted upon or reviewed. Indeed, no legitimate business would need hundreds of "consultants" to advise it on the same topic.

26. Parke-Davis did, however, routinely analyze whether the consultants meetings were successful in getting the attendees to change their prescription writing practices. At some meetings, the "consultants" were directly asked if they would write more Neurontin as a result of the meeting. Such a question would have been irrelevant if the actual purpose of the meeting was to receive the "consultants'" advice. Parke-Davis also routinely tracked consultants' Neurontin prescription writing practices after these meetings. Using market data purchased from third parties, Parke-Davis analyzed whether the doctors they had paid had in fact written more Neurontin prescriptions after the meeting. Again, such data was only relevant if the real purpose of the payments was to influence the doctors to order more Neurontin.

27. A typical consultants' meeting was held in Jupiter Beach, Florida for neurologists from the North East CBU during the weekend of April 19-21, 1996. The "consultants" selected for this meeting were not chosen on the basis of their consulting acumen, but because of their potential to write Neurontin prescriptions. In a memorandum announcing the event to Parke-Davis personnel, the Neurontin Marketing Team acknowledged that in order to target neurologists with the greatest potential for writing Neurontin prescriptions, sales personnel must select potential attendees from a list of the top prescription writers for anti-epileptic drugs in the Northeast; only persons who fell within this desirable demographic were allowed to be invited. A copy of the Neurontin Marketing Team memorandum is attached as Exhibit 1.

28. Qualifying physicians were given a round-trip airfare to Florida (worth \$800.00), two-nights accommodations (worth \$340.00), free meals and entertainment, ground transportation and a "consultant's fee" of \$250.00. Ample time was provided so that the Parke-Davis consultants could enjoy the beach resort. The value of the junket was approximately \$2,000.00 per physician.

29. The Jupiter Beach consultants' meeting included two half days of presentations by Parke-Davis relating to Neurontin, including extensive presentations relating to off-label uses. Although technically the presentations were provided by an independent company, Proworx, all aspects of the presentation were designed, monitored, and approved by Parke-Davis. It selected the speakers, picked the presentation topics and previewed the content of the presentations to make sure that they were acceptable. Parke-Davis paid all expenses relating to the Consultants' meeting including all payments to the attendees and the presenters, all travel, accommodation, meals and entertainment expenses, all presentation expenses, all expenses and fees incurred by Proworx, and the substantial fees paid to the presenting physicians. Notwithstanding the FDA's prohibition

regarding the provision of promotional materials on off-label uses, Parke-Davis provided written abstracts of the presentations that detailed off-label use of Neurontin to each of its “consultants.”

30. No effort was made to obtain professional advice at Jupiter Beach from the “consultants” Parke-Davis had wined, dined, and entertained during the weekend. A follow-up memorandum to Parke-Davis marketing officials noted that “the participants were delivered a hard hitting message about Neurontin” and emphasized that the participants were encouraged to use Neurontin at higher doses. See Exhibit 2. More importantly, after the conference Parke-Davis generated “trending worksheets” listing the doctors who attended the consultants’ meeting. These worksheets enabled Parke-Davis to track Neurontin prescription habits of the attendees before and after the consultant’s meetings to determine if these “high writing” prescribers wrote more Neurontin scripts after the conference. See Exhibit 3. Persuading these heavy prescribers to order more Neurontin for their patients was, in fact, the sole purpose of the Jupiter Beach junket. A list of the attendees and presenters at the Jupiter Beach Consultants’ Meeting is attached as Exhibit 4.

31. Jupiter Beach was not unique. Parke-Davis hosted dozens of consultants’ meetings between late 1995 and 1997 in which the “consultants” received payments and gratuities as well as presentations on off-label Neurontin use designed to change the physicians’ prescription writing habits. Comparable consultants’ meetings included, but were not limited to, the following:

Topic	Location	Dates
Mastering Epilepsy	La Costa Resort, CA	July 20-23, 1995
Mastering Epilepsy	Santa Fe, New Mexico	Nov. 16-19, 1995
Neurontin Consultants Conference	Marco Island, Fla	February 2-4, 1996
Pediatric Epilepsy	Hutchinson Island, Fla	February 9-11, 1996

Mastering Epilepsy Science	Walt Disney World, FL	Feb. 22-25, 1996
Pediatric Epilepsy	Hutchinson Island, Fla	March 8-10, 1996
Mastering Epilepsy	Ritz Carlton, Aspen, CO	April 18-21, 1996
Affective Disorders in Psychiatry	Marco Island, FL	April 20, 1996
Affective Disorder Consultants Conference	Southern Pines, NC	April 27, 1996
Neuropathic Pain Conference	Palm Beach, FL	May 11, 1996
Regional Consultants Conference	Ritz Carlton, Boston, MA	May 10-11, 1996
Epilepsy Management Advisors Meeting	Sheraton Grande Torrey Pines, La Jolla, CA	June 21-23, 1996
Epilepsy Management	Rancho Bernardo, CA	June 28-30, 1996
Use of Anti-Convulsants in Psychiatric Disorders	Short Hills, N.J.	Oct 18-19, 1996
Non-epileptic Uses of Neurontin	Longboat Key, FL	Nov. 6, 1996
Neurological Conditions Conference	Ritz Carlton, Atlanta, GA	Sept. 27-28, 1997

Other consultants' meetings took place at Charleston, S.C., Coconut Grove, FL, Naples, FL, Memphis, TN, Louisville, KY, Washington, D.C., Aspen, CO, and other places. Hundreds, if not thousands, of physicians received kickbacks to attend these events.

32. Not all payments to consultants were made at conferences as elaborate as Jupiter Beach. Many consultants' meetings consisted of lavish dinners at local restaurants. The emphasis on these meetings was also on off-label uses, and \$200 "honorariums" were paid to the physicians who did nothing for the payment except show up. At none of the events did the consultants provide legitimate consultation to Parke-Davis, but at all of the events the "consultants" were encouraged to increase their Neurontin prescription writing.

Medical Education Seminars

33. Another format where Parke-Davis paid kickbacks to physicians to hear off-label promotion of Neurontin were programs billed as Continuing Medical Education seminars (CME). These conferences and seminars were set up to appear to qualify for an exception to the FDA's off-label marketing restrictions which permits physicians to learn about off-label uses of pharmaceuticals at independent seminars. Such seminars, however, must be truly independent of the drug companies. The companies may make "unrestricted grants" for the purpose of a seminar, but may not be involved in formulating the content of the presentations, picking the speakers or selecting the attendees. None of these requirements were observed with regard to the CME seminars sponsored by Parke-Davis for the promotion of off-label uses of Neurontin. While Parke-Davis retained third party organizations, such as Proworx and Medical Education Systems, to present the event seminars, it had control of virtually every aspect of these events, and the seminar companies obtained Parke-Davis' approval for all content presented at the seminars. Parke-Davis also paid all expenses, including all the seminar companies' fees.

34. Although the seminar companies acted as the conduit for the payments and gratuities given to the physician attendees, like the Jupiter Beach consultants' meetings, Parke-Davis controlled every aspect of the CME programs. It designed and approved the programs; hand-picked the speakers for the seminars; approved the seminar presentations of the seminars; previewed, in most cases, the contents of the seminars prior to delivery; selected the attendees based on their ability and willingness to prescribe high quantities of Neurontin; evaluated the presentations to make sure Parke-Davis' "message" was appropriately delivered; black-listed presenters whose presentations were not sufficiently pro-Neurontin; and monitored the prescribing patterns of the physicians who attended

these conferences to insure the purpose of the conference—increased writing of Neurontin prescriptions—was achieved. Follow-up reports to marketing executives at Parke-Davis highlighted that the attendees received presentations regarding off-label marketing and recommendations for dosages larger than those labeled effective by the FDA. These memoranda also reported to senior executives the pledges made by attendees to order more Neurontin for their patients.

35. For some seminars, high prescription writing physicians were selected to receive junkets comparable to those Parke-Davis provided to the attendees of the Jupiter Beach consultants' meetings. Others were less lavish, but physicians received free tuition, free accommodations, free meals, and cash. Frequently the Parke-Davis CME seminars were accredited by continuing medical education organizations, which meant that the physicians taking advantage of Parke-Davis' junkets did not have to pay tuition or spend additional time to fulfill their continuing medical education licensure requirements by attending truly independent medical education programs.

36. Representative CME programs sponsored by Parke-Davis where it paid extensive kickbacks to attending physicians, included, but are not limited to, the following:

Seminar	Location	Date
Merritt-Putnam Epilepsy Postgraduate Course		Jan. 19, 1996
Merritt-Putnam Seminar	Chicago, IL	January 26, 1996
New Frontiers in AntiEpileptic Drug Use	California	Sept-Oct 1996
Diabetic Neuropathy	Ritz Carlton, Boston, MA	June 22-24, 1997
Merritt Putnam Symposium	Key Biscayne, FL	September 11, 1997
Merritt Putnam Conference on Monotherapy	Palm Springs, CA	September 19, 1997

Merritt-Putnam Conference on Monotherapy	St. Louis, MO	October 3, 1997
Merritt-Putnam Symposium	Boston, MA	December 5, 1997

Grants and “Studies”

37. Parke-Davis also made outright payments, in the form of grants, to reward demonstrated Neurontin believers and advocates. Parke-Davis sales managers identified key doctors who actively prescribed Neurontin or programs which were willing to host Neurontin speakers and encouraged such persons or programs to obtain “educational grants” from Parke-Davis. Under this program of kickbacks Parke-Davis paid:

- \$2,000.00 to Berge Ninmpolan, MD, “a great Neurontin believer,” to attend a neurology seminar in San Francisco, in March 1996.
- \$1,000.00 to the University of Texas at Houston Department of Neurology to host a symposium where presentations would be made regarding successful off-label treatment with Neurontin.
- \$3,000.00 to the University of Texas Medical School to host a conference in August 1996 at which a well-known specialist in epilepsy, who prescribed Neurontin, would attend.
- \$4,000.00 to pay for a neurologist from the University of Texas at San Antonio to attend the American Epilepsy Society Conference in December 1996, a conference at which Parke-Davis was presenting extensive documentation on off-label uses for Neurontin.

- \$2,500.00 to the University of Texas in Houston to bring Dr. B.J. Wilder to the campus to hold a seminar. Dr. Wilder was one of Neurontin's biggest boosters for off-label indications and had been paid tens of thousands of dollars to promote Neurontin's off-label uses for Parke-Davis across the country.
- \$2,500.00 in June 1996 to pay for representatives from the University of Pennsylvania Medical Center to attend a conference in Saint Petersburg, Russia on the utilization of anti-epileptic drugs, including Neurontin.
- \$5,000.00 to Dr. Alan B. Ettinger, of Stonybrook, N.Y. in December 1996, a physician who had informed Parke-Davis that he was interested in possibly doing research in Neurontin and maintained a database of patients who were treated with Neurontin.
- \$500 to Bruce Ehrenberg, of Boston, MA, a leading speaker for Parke-Davis regarding off-label use of Neurontin, to attend a conference in China.
- \$1000 to Israel Abrams, M.D., Paul C. Marshall, M.D., Beth Rosten, M.D. and Spencer G. Weig, of Worcester MA, for educational programs in February 1996. According to the local Parke Davis representative requesting the grant, "much of the Neurontin success in Worcester has been attributed to . . . the 4 pedi epileptologists below".
- \$1400 to Dr. Ahmad Beydoun of Ann Arbor, MI for post-graduate training in March 1996. This grant was processed on a quick turnaround, the Parke-Davis representative noting "I realize that this is a very short time line; however, Dr. Beydoun is a very important customer".

- \$1,500 to Jim McAuley, R.Ph, Ph.D. for educational materials relating to epilepsy. Parke-Davis decided to provide the funds because McAuley was an advocate of Neurontin and he was important in getting another Parke-Davis drug, Cerebyx, accepted on the formulary for Ohio State University.
- A grant in an unknown amount to University Hospital in Cleveland in exchange for the hosting programs regarding Neurontin's use in treating neuropathic pain at conferences specifically devoted to obtaining referrals from other doctors.

38. These grants, and others, were charged to the Neurontin marketing budget. Each of these grants were made solely because an individual who would receive the money was a large Neurontin supporter or would host a program where a well known Neurontin supporter would recommend that other physicians increase their prescriptions of Neurontin. Each of these grant awards constituted a reward or kickback for the recipient's advocacy of Neurontin.

39. Parke-Davis' medical liaisons informed leading Neurontin subscribers that significant advocacy for Neurontin would result in the payment of large grants. These studies did not involve significant work for the physicians. Often times they required little more than collating and writing up office notes or records. Indeed, as noted below, Parke-Davis frequently hired technical writers to write the articles for which the "authors" had been given grants.

40. Parke-Davis was aware that these articles and studies provided minimal scientific benefit. In a letter to the FDA in June 1997, Parke-Davis submitted a list of "studies relating to pain, pain syndromes, and psychiatric disorders" which failed to include any of these numerous studies, purportedly funded by Parke-Davis. Parke-Davis intentionally neglected to report these "studies" to the FDA because they knew the funded "research" had no scientific value and would not be deemed

to be studies by the FDA. Payments Parke-Davis made for “studies” included, but were not limited to the following:

Funded Project	Payee	Payment
Statistical Analysis of Patients Treated With Neurontin For Pain	Hans Hansen, M.D.; Statesville, NC	\$7,000.00
Reduction of Sympathetically Medicated Pain and Sudomotor Function	David R. Longmire, M.D.; Russellville, AL	\$7,000.00
Data entry for Neurontin and Pain Analysis	Travis Jackson, M.D., David Meyer, M.D.; Winston-Salem, NC	
Trial of Neurontin for distal symmetric polyneuropathy associated with AIDS	Joseph Weissman, M.D. Atlanta, GA	\$20,000.00
Neurontin for neuropathic pain in chronic pain syndromes	Lavern Brett, M.D. Washington, D.C.	\$25,000.00
Retrospective chart analysis of Neurontin use with bipolar disorder patients	Ralph S. Rybeck, M.D.	\$5,000.00
Retrospective Analysis of Neurontin in the treatment of pain	David R. Longmire, M.D.; Russellville, AL	\$2,000.00
Retrospective Analysis of Neurontin in the treatment of chronic pain	Don Schanz, D.O. Traverse City, MI	\$8,000.00
Case histories relating to use of Neurontin as an adjuvant analgesic	Elizabeth J. Narcessian, M.D; W. Orange, NJ	\$4,000.00

Plaintiff has reason to believe that other payments were made to physicians for other “studies” of questionable scientific credibility.

41. One particularly large study conducted by Parke-Davis served as yet another engine to financially reward physicians for prescribing Neurontin. In 1995 and 1996 Parke-Davis conducted an enormous Phase IV trial known as STEPS. Although STEPS took the form of a research clinical

trial, it was, in fact, a marketing ploy designed to induce neurologists to become comfortable prescribing Neurontin at a far higher dose than indicated in the FDA approved labeling. While most clinical studies have a limited numbers of investigators treating a number of patients qualified for the study, the STEPS protocol called for over 1,200 "investigators" to enroll only a few patients each. The participating physicians were instructed to titrate their patients to higher than labeled dosages of Neurontin to demonstrate that patients could tolerate high dosages of the drug. Rewarding physicians for prescribing high doses on Neurontin was another way to increase Neurontin sales because higher per patient dosages increased the amount of Neurontin sold. Additionally, the STEPS study was also designed to habituate physicians to place non-study patients on Neurontin on doses higher than found effective in the clinical trials monitored by the FDA.

42. Physicians enrolling in the STEPS study were paid for agreeing to participate in the study and for every patient enrolled. At the conclusion of the study Parke-Davis offered each of the 1,200 investigators additional cash for each patient the doctor kept on Neurontin after the study ended. These payments were unquestionably kickbacks, each participating doctor was expressly paid for writing Neurontin prescriptions for their patients. The number of investigators who received such payments are too many for the Relator to list. Additionally, Parke-Davis has exclusive control of the information regarding who received such payments at the conclusion of the STEPS trial.

Payments to "Authors" of Ghost Written Articles

43. Yet another method of rewarding doctors for their advocacy of Neurontin was to pay them honorarium for lending their names to scientific articles which were actually prepared and written by third parties retained by Parke-Davis. In 1996 Parke-Davis retained AMM/ADELPHI, Ltd. and Medical Education Systems, Inc., to prepare no less than twenty (20) articles for publication in

various neurology and psychiatry journals. Most of these articles concerned off-label usage of Neurontin and were generated so that Parke-Davis would have completely controlled publications it could distribute pursuant to its "publication strategy". The content of these articles were actually written by non-physician technical writers retained by Parke-Davis, and Parke-Davis had the right to control the content of all of the articles. Parke-Davis paid all expenses in connection with the creation of these publications.

44. Once Parke-Davis and the technical writers conceived the articles, Parke-Davis and its outside firms attempted to find recognized Neurontin prescribers whose names could be used as the authors of these articles. In some cases, drafts of the articles were completed even before an "author" agreed to place his or her name on the article. This even occurred in connection with case histories that purported to describe the "author's" personal treatment of actual patients. The "authors" were paid an honorarium of \$1,000.00 to lend their names to these articles, and also were able to claim publication credit on their curriculum vitae.

45. After the technical writers completed their work, Parke-Davis and its outside firms found journals that would publish the articles. Parke-Davis' role in creating, approving and sponsoring the articles was hidden from the public. While the articles might reference that the author received an honorarium from the outside firm, the articles failed to state that the honorarium was paid with money provided by Parke-Davis and that Parke-Davis had approved the content and hired the actual authors. For example, an article created by Medical Education Systems (MES), *Gabapentin and Lamotrigine: Novel Treatments for Mood and Anxiety Disorders*, published in CNS Spectrums noted that "an honorarium was received from Medical Education Systems for preparation of this

article”, but never revealed Parke-Davis’ retention and payment of MES or the fact that MES personnel, while under contract to Parke-Davis, wrote the article. See Exhibit 5 attached hereto.

46. Parke-Davis used these publications as part of their “publication strategy” by presenting the articles as evidence of independent research conducted by persons with no monetary interest in Neurontin. This impression, of course, was false. Parke-Davis created the article to promote off-label uses for Neurontin, purchased the names and reputations of the authors with kickbacks and controlled the content of the article. Documents identifying the twenty (20) articles and the persons who received payments for lending their names to these articles are attached as Exhibit 6.

Speakers’ Bureau

47. Parke-Davis also formed the Speakers Bureau, another method to make large and numerous payments to physicians who recommended Neurontin at teleconferences, dinner meetings, consultants meetings, educational seminars, and other events. These speakers repeatedly gave short presentations relating to Neurontin which they were paid anywhere from \$250.00 to \$3,000.00 per event. Speakers such as Steven Schachter, B.J. Wilder, Ilo Leppik, Gary Mellick, David Longmire, Gregory Bergey, Michael Merren, David Treiman, Michael Sperling, Martha Morrell, R. Eugene Ramsay, John Pellock, Ahmad Beydoun, Thomas Browne, John Gates, Jeffrey Gelblum, Dennis Nitz, Robert Knobler and others received tens of thousands of dollars annually in exchange for recommending to fellow physicians that Neurontin be prescribed, particularly for off-label uses. The payments that these doctors received were far in excess of the fair value of the work they performed for Parke-Davis. Speakers who most zealously advocated Neurontin were hired most frequently for speaking events, notwithstanding the fact that many of these events purported to be independent

medical education seminars where independent information was supposed to be delivered. The identity of the doctors in the speakers bureau who received kickbacks through excessive compensation can only be determined after review of the records in the exclusive custody of the Defendant. Plaintiff is aware that extensive payments through the Speakers' Bureau took place between 1995 and 1997, the last year for which plaintiff has had access to records. Plaintiff is aware that off-label promotion of Neurontin pursuant to the "publication strategy" continued after 1997 and accordingly believes such kickback payments continued through 2000.

48. Parke-Davis' marketing personnel, including its medical liaison staff, informed physicians of the lucrative rewards of joining the Neurontin Speaker's Bureau. Physicians were informed that if they prescribed enough Neurontin, they, too, could also be eligible for receiving substantial payments just for describing their clinical experience to peers at events dedicated to promoting Neurontin's off-label uses. Parke-Davis marketing personnel, however, made it clear that the only way the doctors could receive such cash payments was if they prescribed substantial amounts of Neurontin to their patients, preferably for off-label uses.

49. Parke-Davis either knew that the payments described above constituted kickbacks or acted in reckless disregard of laws and regulations of which it was aware. Parke-Davis was well aware of the Medicare and Medicaid Fraud and Abuse laws, which included the Medicaid anti-kickback statute. It was further aware that the safe harbors established by the Department of Health and Human Services did not cover the extensive payments it made to doctors. Parke-Davis was aware that its payments did not comply with the AMA's guidelines for payments to physicians. It also knew that the payments had been made for the express purpose of encouraging the physicians to order Neurontin for their patients. Parke-Davis was also aware of the Inspector General's Special Fraud

medical education seminars where independent information was supposed to be delivered. The identity of the doctors in the speakers bureau who received kickbacks through excessive compensation can only be determined after review of the records in the exclusive custody of the Defendant. Plaintiff is aware that extensive payments through the Speakers' Bureau took place between 1995 and 1997, the last year for which plaintiff has had access to records. Plaintiff is aware that off-label promotion of Neurontin pursuant to the "publication strategy" continued after 1997 and accordingly believes such kickback payments continued through 2000.

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Alert which raised particular concerns about drug marketing. Nonetheless, Parke-Davis did nothing to curb its kickback payments to physicians, and could not have marketed Neurontin's off-label uses without such payments.

50. In 1997 in the wake of an investigation by the FDA, Parke-Davis conducted a review of its marketing practices in light of existing Medicaid kickback regulations. As a result of that review, Parke-Davis determined that none of the programs described above should have been conducted in the manner previously conducted by Parke-Davis. Parke-Davis issued guidelines to comply with Federal Regulations which essentially prohibited each of the programs described above. Nonetheless, the payments to physicians for the off-label marketing of Neurontin did not cease and the programs continued at least until 1998. Given that Parke-Davis's records demonstrate payments of inappropriate kickbacks to doctors through 1998, Plaintiff believes that such payments continued through the merger of Parke-Davis' parent, Warner-Lambert, with Defendant Pfizer, or perhaps even through the calling of a grand jury regarding Parke-Davis's marketing practices relating to Neurontin.

D. Parke-Davis's use of Medical Liaisons to Promote Neurontin Off-Label.

51. Parke-Davis's normal sales force was not permitted to promote off-label uses of Neurontin to its physician customers. The FDA, however, permitted drug company representatives to provide balanced, truthful information regarding off-label usage if specifically requested by a physician and if there was no attempt to solicit such information by the drug company. Commencing in 1995 Parke-Davis increasingly hired medical liaisons and trained them to aggressively solicit requests for off-label information from physicians. Once this door was open, Parke-Davis trained the medical liaisons to engage in full scale promotion of Neurontin's off-label uses, including repetition of non-scientific, anecdotal information designed to convince physicians that off-label usage of

Neurontin was safe and effective. In effect, Parke-Davis used the medical liaisons as a surrogate sales force who had the liberty to solicit physicians regarding off-label uses. Indeed, medical liaisons were selected and promoted based on their ability to sell and sales training was encouraged.

52. Parke-Davis knew this use of medical liaisons was inappropriate. When he was hired by Parke-Davis in March 1996, Relator was specifically questioned about whether he had difficulty working in gray areas or bending rules. High level personnel within Parke-Davis acknowledged to Relator that the use of medical liaisons by the South Central, North Central and North East CBUs were thinly disguised methods of evading the FDA's policies on off-label promotion.

53. Similarly, on April 16, 1996, at a training session for medical liaisons Parke-Davis in-house lawyers stopped the video taping of a medical liaison training sessions to advise the liaisons that notwithstanding formal policies to the contrary, liaisons could cold call on physicians so long as they had executed request forms (forms that supposedly verified that the physician had initiated the meeting) at the end of the call. Moreover, the liaisons were informed that the request forms could be filled out by Parke-Davis sales representatives instead of the doctors. Company lawyers also informed the liaisons in training that there was no need to present balanced information to the customers, and that liaisons should always remember that sales were necessary in order to keep the company profitable. The liaisons were also informed by the lawyers, off camera, that there really was no definition of "solicitation" and that there were methods to induce the physicians to inquire about off-label uses. In effect, once the medical liaison got a meeting with a doctor, there were ways to get the information about off-label uses to the doctor even if the physician had not requested off-label information. The lawyers also warned the liaisons under no circumstances should any information about off-label uses be put in writing.

54. Medical liaisons were instructed in the clearest possible terms that they were to market and sell Neurontin based on its off-label uses. On a teleconference on May 24, 1996, John Ford, a senior marketing executive at Parke-Davis' Morris Plains headquarters directly informed the medical liaisons that in order to market Neurontin effectively, Neurontin had to be marketed for monotherapy, pain, bipolar disease, and other psychiatric uses, all of which were off-label. Ford conceded that such marketing had to be primarily performed by the medical liaisons, because they were the only one who could discuss these matters. At another meeting with the medical liaisons, Ford was even blunter:

"I want you out there every day selling Neurontin. Look this isn't just me, it's come down from Morris Plains that Neurontin is more profitable. . . . We all know Neurontin's not growing adjunctive therapy, beside that is not where the money is. Pain management, now that's money. Monotherapy, that's money. We don't want to share these patients with everybody, we want them on Neurontin only. We want their whole drug budget, not a quarter, not half, the whole thing. . . . We can't wait for them to ask, we need to get out there and tell them up front. . . . That's where we need to be holding their hand and whispering in their ear Neurontin for pain, Neurontin for monotherapy, Neurontin for bipolar, Neurontin for everything. . . . I don't want to see a single patient coming off Neurontin until they have been up to at least 4800mg/day. I don't want to hear that safety crap either, have you tried Neurontin, every one of you should take one just to see there is nothing, it's a great drug."

55. Thus, Relator and the other medical liaisons were trained to cold call high decile physicians (those who saw the most patients in a given specialty), and sell them on the off-label benefits of Neurontin. A key aspect of this selling was misrepresentation. The first thing to be misrepresented was usually the status of the medical liaisons. With the full approval of marketing officials at Parke-Davis such as John Ford, Phil Magistro, and John Krukar, medical liaisons were routinely introduced as specialists in the specific drug they were presenting at a particular meeting. Thus, medical liaisons could be experts in anti-epileptic drugs at one moment and an hour later be an expert in cardiac medication. Medical liaisons were also encouraged to represent themselves as

medical researchers, even though they neither conducted medical research nor analyzed medical research performed by others. It was not uncommon for medical liaisons to be introduced as physicians, even though they had no such qualifications. Sales personnel were instructed to introduce medical liaisons as scientific employees who were given momentary leave of their academic duties to make an individual presentation to the physician; the fact that the liaisons were part of Parke-Davis standard marketing detail was intentionally hidden.

56. Extensive misrepresentations were also made regarding the scientific information concerning off-label usage of Neurontin. The following misrepresentations relating to off-label usage of Neurontin were routinely made to high decile physicians in the North East and other CBUs with the knowledge and consent of persons such as Phil Magistro, John Krukar, and other marketing personnel at Parke-Davis. In 1995 and 1996 the medical liaisons were trained to make such misrepresentations. Given that medical liaisons were trained to make such statements by senior personnel, Realtor believes such conduct continued after he left the company in July 1996.

1. *Bipolar Disorder.* Medical Liaisons informed psychiatrists that early results from clinical trials evaluating Neurontin for the treatment of bipolar disorder indicated a ninety percent (90%) response rate when Neurontin was started at 900mg/day dosage and increased to a dosage of 4800mg/day. No such results existed. Nor was any type of clinical trial being conducted other than a pilot study. There were no clinical trials or studies indicating that Neurontin was safe or effective up to 4800mg/day. Indeed, Parke-Davis was in possession at this time of clinical trial evidence which showed that there was no dose response difference between patients who received 600 mg, 1200 mg and 2400 mg/day. Any data relating to the use of Neurontin in bipolar disorder

was strictly anecdotal and of nominal scientific value. Indeed, most of the published reports on this topic had been written and commercially sponsored by Parke-Davis, although this fact was hidden. Medical liaisons were trained to inform psychiatrists that there were no reports of adverse effects for Neurontin when used for psychiatric purposes. In fact, such reports had been reported to Parke-Davis personnel but Parke-Davis attempted to hide such reports from physicians.

2. *Peripheral Neuropathy, Diabetic Neuropathy, and Other Pain Syndromes.*

Medical liaisons were trained and instructed to report that “leaks” from clinical trials demonstrated that Neurontin was highly effective in the treatment of various pain syndromes and that a ninety percent (90%) response rate in the treatment of pain was being reported. No such body of evidence existed. Nor was there any legitimate pool of data from which a response rate, much less a ninety percent (90%) response rate, could be calculated. Medical liaisons were trained to claim support for these findings as a result of inside information about clinical trials where no such information existed. The only support for these claims were anecdotal evidence of nominal scientific value. Many of the published case reports had been created and/or sponsored by Parke-Davis in articles which frequently hid Parke-Davis’s involvement in the creation of the article. Parke-Davis’s payment for the creation of these case reports was also hidden from physicians.

3. *Epilepsy Monotherapy.* Medical liaisons were strongly encouraged to push neurologists to prescribe Neurontin as the sole medication to treat epilepsy, even though studies only found it safe and effective as adjunctive therapy. Medical liaisons

were trained to inform neurologists that substantial evidence supported Parke-Davis' claim that Neurontin was effective as monotherapy. In fact, at this time, Parke-Davis knew that clinical trials regarding Neurontin's efficacy as a monotherapy were inconclusive. One of Parke-Davis' clinical trials, 945-82, demonstrated that Neurontin was not an effective monotherapy agent; the vast majority of patients in the study taking Neurontin were unable to continue with Neurontin alone. The same study showed that there was no effective difference between administration of Neurontin at 600, 1200 or 2400mg. Notwithstanding this data, the company continued to claim that physicians should use Neurontin at substantially higher doses than indicated by the labeling. Indeed, although medical liaisons routinely claimed Neurontin to be effective as monotherapy, in 1997 the Food and Drug Administration refused to find Neurontin to be a safe and effective monotherapy.

4. *Reflex Sympathetic Dystrophy ("RSD")*. Medical liaisons informed physicians that extensive evidence demonstrated the efficacy of Neurontin in the treatment of RSD. The only such evidence that existed was anecdotal reports of nominal scientific value. Medical liaisons were trained to refer to case reports, most of which had been created or sponsored by Parke-Davis, as "studies."

5. *Attention Deficit Disorder ("ADD")*. Medical liaisons were instructed to inform pediatricians that Neurontin was effective for the treatment of ADD. No data, other than occasional anecdotal evidence, supported this claim. Nonetheless, the medical liaisons were trained to report that large number of physicians had success treating ADD with Neurontin, when no such case reports existed.

6. *Restless Leg Syndrome ("RLS")*. RLS was another condition where Parke-Davis medical liaisons were trained to refer to a growing body of data relating to the condition, when no scientific data existed. The only reports were anecdotal, most of which had been created and/or sponsored by Parke-Davis.
7. *Trigeminal Neuralgia*. Although medical liaisons represented that Neurontin could treat Trigeminal Neuralgia, again no scientific data supported this claim with the exception of occasional anecdotal reports. No data demonstrated that Neurontin was as effective as currently available pain killers, most of which were inexpensive.
8. *Post-Herpatic Neuralgia ("PHN")*. Medical liaisons were trained to tell physicians that seventy-five percent (75%) to eighty percent (80%) of all PHN patients were successfully treated with Neurontin. Once again, no clinical trial data supported such a claim.
9. *Essential Tremor Periodic Limb Movement Disorder ("ETPLMD")*. Medical liaisons were trained to allege that Neurontin was effective in the treatment of these conditions. No scientific data supported such claims with the exception of anecdotal reports of nominal scientific value.
10. *Migraine*. Claims that Neurontin was effective in the treatment of migraine headaches were made by the medical liaisons and were supposedly based on early results from clinical trials. Although pilot studies had been suggested and undertaken, no early results of clinical trials existed to support these claims. Once again, any data relating to treatment of migraines was purely anecdotal and of nominal scientific value. Most of the case reports were either created or sponsored by Parke-Davis.

11. *Drug and Alcohol Withdrawal Seizures.* Medical liaisons suggested that Neurontin be used in the treatment of Drug and Alcohol Withdrawals despite the lack of any data supporting Neurontin as an effective treatment for these conditions.

57. The representations stated above were routinely made to high decile physicians in the North East CBU and other CBUs. Lists of high decile physicians who were targeted to hear the standard medical liaisons approaches, which included the misrepresentations identified in the preceding paragraphs, are attached as Exhibit 7. The lists attached as Exhibit 7 are not definitive or exhaustive. Relator does not know all the physicians to whom all the representations were made and could not possibly know all the names because the information is within the custody and control of Defendant. In addition to himself, Relator is aware that such misrepresentations were made to physicians by Michael Davics, Joseph McFarland, Phil Magistro, Lisa Kellett, Joseph Dymkowski, Daryl Moy, Richard Grady, Ken Lawler and others. Although Relator did not witness medical liaisons from CBUs other than the North East making such representations, because such personnel were trained with him, he believes that the CBU's medical liaisons also delivered the misrepresentations described above as part of their standard pitch on off-label uses.

58. Not all physicians on the lists attached as Exhibit 7 would have received all of the misrepresentations described above. Each specialist would have received the misrepresentations relating to his or her practice. If physician's practice focused on epilepsy, that doctor would not have received information relating to the treatment of ADD, but he or she would have received misrepresentations relating to monotherapy. Regardless of the specialty, unsupported claims of effectiveness for off-label usage was a key portion of medical liaisons presentations relating to Neurontin.

59. Misrepresentations by Parke-Davis were not limited to presentations by medical liaisons. As noted above, publications Parke-Davis distributed as part of its "publication strategy", intentionally misrepresented Parke-Davis' role in the creation and sponsorship of the publications. Physicians were led to believe that the publications were the independent, unbiased research of the authors of the articles. In fact, many of the publications distributed to physicians were created by Parke-Davis and written by third parties retained by Parke-Davis who were under Parke-Davis's control. The fact that these articles were authored by ghost writers retained by Parke-Davis was intentionally hidden, and the fact that the authors had financial ties to Parke-Davis was also intentionally undisclosed. For example, an article widely circulated by Parke-Davis concerning the use of Neurontin in the treatment of Restless Leg Syndrome asserted that the authors Gary A. Mellick and Larry B Mellick, had not and never would receive financial benefit from anyone with an interest in Neurontin, yet the Mellick brothers had received tens of thousands of dollars for acting as speakers at Parke-Davis events. This financial connection was hidden from the persons who received copies of the Mellick brothers' articles.

E. Parke-Davis' Causation of False Claims.

60. Parke-Davis knew that one quarter to one-third of all Neurontin prescriptions in the United States were paid for by the Medicaid program. Parke-Davis even targeted Medicaid patients as a growth market for Neurontin. Parke-Davis was aware that most of the high decile physicians who they so eagerly targeted, relied heavily on Medicaid for payment. This is not surprising because Parke-Davis was aware that many high volume practices contained a disproportionate share of Medicaid patients.

61. Each physician and pharmacist that participates in Medicaid must sign a provider agreement with his or her state. Although there are variations in the agreements among the states, all states require the prospective Medicaid provider to agree that he/she will comply with all Medicaid requirements, including the fraud and abuse provisions and anti-kick back provisions. Some states, such as Florida, have provider agreements that expressly provide that the submission of a Medicaid claim is an express certification that the provider has complied with all Medicaid requirements, including Medicaid anti-kickback provisions. In other states, such as Massachusetts, the Medicaid claim form itself contains a certification by the provider that the provider has complied with all aspects of the state Medicaid program, including compliance with Federal Regulations. In these states, submission of a Medicaid claim is an express certification by the provider that the services for which reimbursement are sought are eligible for Medicaid reimbursement and that the provider has complied with all Medicaid requirements, including compliance with the anti-kickback provisions.

62. Even in those states in which submission of a Medicaid claim does not constitute an express certification, the Medicaid Provider Agreement conditions participation in the Medicaid Program with compliance with all state and federal Medicaid statutes and regulations. A provider who fails to comply with these statutes and regulations is not entitled to payment for services rendered to Medicaid patients. By submitting a claim for Medicaid reimbursement in these states, the provider implicitly certifies that the submitted claim is eligible for Medicaid reimbursement and that the provider is in compliance with all state and federal Medicaid requirements including compliance with the anti-kickback regulations.

63. To summarize, pursuant to the terms of each state's provider agreements or the claim forms used to submit claims, all pharmacists and physicians expressly or impliedly certify that the claims they have submitted are eligible for Medicaid payment and that the providers have complied with the statutes and regulations relating to Medicaid including compliance with the Medicaid anti-kickback provisions.

64. Medicaid claims for the payment of off-label Neurontin prescriptions are filed with the states by the pharmacists who fill the Medicaid patients' prescriptions. In most cases, the pharmacist will not know whether the prescription is on-label or off-label, and consequently, does not know whether the prescription is for a medically acceptable use, and consequently, a covered outpatient drug under Medicaid. Nonetheless, because such prescriptions are not eligible for Medicaid reimbursement, submission of such a claim for reimbursement constitutes a false claim for the purposes of 31 U.S.C. § 3729. A pharmacist who does not know the claim is ineligible has not knowingly submitted a false claim and is not liable to the United States pursuant to § 3729(a). However, a person who *knowingly causes* such a claim to be filed is liable for causing a false claim pursuant to § 3729.

65. Parke-Davis knew that off-label prescriptions of Neurontin were not eligible for Medicaid reimbursement. Parke-Davis' former corporate parent, Warner-Lambert, had entered into a Medicaid Rebate Agreement with the United States which specifically informed Parke-Davis what constituted covered outpatient drugs under Medicaid, and notified Parke-Davis that drugs that were not used for a medically accepted use were not covered outpatient drugs. Parke-Davis was also aware of the passage of 42 U.S.C. § 1396r-8 and its limitations on Medicaid reimbursement for prescription drugs. Notwithstanding Parke-Davis's knowledge that off-label prescriptions of Neurontin were not

medically accepted uses eligible for Medicaid reimbursement, Parke-Davis knowingly and intentionally took steps to increase the number of off-label Neurontin prescriptions submitted to Medicaid. But for Parke-Davis' promotion of off-label uses, most of the ineligible claims for payment of Neurontin prescriptions would have never been filed. Every off-label Neurontin prescription caused by Parke-Davis's off-label promotion of Neurontin is a false claim caused by Parke-Davis for the purposes of 31 U.S.C. § 3729.

66. Submission of a Medicaid claim for reimbursement of a Neurontin prescription that has been induced by a kickback under the Medicaid anti-kickback provisions is also a false claim because the Medicaid program, if it was aware of the kickback, would not pay such a claim. Further, a physician who seeks payment from Medicaid for his treatment of a Medicaid patient for whom he or she has prescribed a drug as a result of his or her receipt of a kickback has also submitted a false certification. Such a physician is not in compliance with the Medicaid anti-kickback provisions, and is no longer eligible to participate in Medicaid. Had the federal or state Medicaid officials known that the physician had accepted kickbacks, the physician's claim for treatment of the patient would not be paid. A physician who has accepted kickbacks and knowingly seeks payment from Medicaid for claims related to the kickback is liable for violation of the False Claims Act.

67. Additionally, the person who pays the kickback is equally liable for this type of false claim. Payment of the kickback inevitably causes the recipient Medicaid provider to submit a false certification – the payment of the kickback causes the provider's Medicaid claims to be ineligible because the provider is no longer in compliance with the anti-kickback provisions. Had the payor not paid the kickback, the provider would not have submitted ineligible claims. The person who pays the kickback is as equally responsible as the receiver of the kickback for the resulting false claim.

68. For the reasons set forth above, Parke-Davis knew that its payments to physicians set forth in Section III.C were kickbacks and that any of those physicians who participated in the Medicaid program would subsequently file false claims. Every Medicaid claim submitted by a physician who took a Neurontin kickback from Parke-Davis is a false claim caused by Parke-Davis for the purposes of 31 U.S.C. § 3729 .

COUNT I

FALSE CLAIMS CAUSED BY KNOWING PROMOTION OF PRESCRIPTION SALES INELIGIBLE FOR MEDICAID REIMBURSEMENT

69. Relator repeats and re-alleges each and every allegation contained in Paragraphs 1 through 68 as if alleged herein.

70. Parke-Davis has caused the submission of hundreds of thousands of false claims by knowingly promoting to Medicaid providers sales of Neurontin for off-label uses which were not eligible for Medicaid reimbursement. Every prescription for Neurontin which was not written for medically acceptable use that was submitted to Medicaid, constitutes a false claim. Parke-Davis is liable, pursuant to 31 U.S.C. § 3729, for each of those false claims which would not have been written but for Parke-Davis' off-label promotion of Neurontin. At the time it engaged in such unlawful promotional activities, Parke-Davis knew that off-label prescriptions for Neurontin were ineligible for Medicaid reimbursement and that its activities would, in fact cause numerous ineligible prescriptions to be submitted to Medicaid. Had Parke-Davis not engaged in such promotions, federal funds would not have been used to pay for prescriptions that were not qualified to be reimbursed by Medicaid.

71. In order to cause ineligible claims to be submitted to Medicaid, Parke-Davis engaged in a systematic and extensive course of fraudulent conduct. This conduct included deliberate disregard of FDA regulations concerning off-label promotion (and conduct designed to hide such disregard from the regulatory authorities), deliberate misrepresentations to physicians of the evidence regarding the safety and efficacy of off-label usage of Neurontin; deliberate payment of tens of thousands of kickbacks to encourage physicians to order Neurontin, and deliberate creation of publications designed to appear to be written by neutral independent researchers, when in fact such publications were created and written by Parke-Davis and its agents, and were the products of substantial undisclosed monetary compensation.

72. Relator cannot identify at this time all of the false claims which were caused by Parke-Davis's conduct. The false claims were submitted by pharmacists with whom the Relator has had no dealings and the records of the false claims are not within the Relator's control. Indeed, specification of the vast number of false claims would be burdensome to the Court and the parties. Given the vast number of false claims, their scope and complexity, Relator is excused from the requirement of specifying each false claim. The time period of the false claims, however was from 1994 through no earlier than 1998, extending, to the best of the Relator's knowledge through the year 2000. Such claims were made across the entire United States.

73. As a result of Parke-Davis actions, the United States has paid directly or indirectly tens of thousands of false claims and spent hundreds of millions of dollars on prescriptions for a medication that has not been proven to be safe or effective. Congress, the federal government, and the individual states never intended to make such payments and would have never made such payments but for the conduct of Parke-Davis. Although Parke-Davis did not submit the claims and

did not directly receive the payments from the states and the United States, Parke-Davis has been the greatest beneficiary from this pattern of unlawful conduct, filling thousands of prescriptions for Neurontin which would have never been placed but for its unlawful conduct.

COUNT II

FALSE CLAIMS CAUSED BY PAYMENT OF KICKBACKS IN VIOLATION OF THE MEDICAID ANTI-KICKBACK PROVISIONS

74. Plaintiff repeats and re-alleges each of the allegations set forth in Paragraphs 1 through 73 as though set forth herein.

75. Parke-Davis has caused the submission of false claims in violation of 31 U.S.C. § 3729 by paying tens of thousand of kickbacks to Medicaid providers, causing the providers to falsely certify that they have complied with the anti-kickback provisions when in fact they had not. Had Parke-Davis not paid kickbacks to these physicians, the physicians would not have falsely certified expressly or implicitly, that they were in compliance with Medicaid anti-kickback provisions. Additionally, had Parke-Davis not paid kickbacks, the pharmacists submitting claims for reimbursement for Neurontin prescriptions that were induced as the result of the payment of kickbacks would not have expressly or implicitly certified that the claims were made in compliance with the rules and regulations concerning the submission of Medicaid claims.

76. Relator cannot identify at this time all of the false claims which were caused by Parke-Davis' conduct. The false claims were submitted by physicians and pharmacists with whom the Relator has had no dealings and the records of the false claims are not within the Relator's control. Indeed, specification of the vast number of false claims would be burdensome to the Court and the parties. Given the vast number of false claims, their scope and complexity, Realtor is excused from

the requirement of specifying each false claim. The time period of the false claims, however was from 1994 through no earlier than 1998, and extending, to the best of the Relator's knowledge, through the year 2000. Such claims were made across the entire United States.

77. As a result of Parke-Davis' actions, the United States has paid directly or indirectly tens of thousands of false claims and spent hundreds of millions of dollars on prescriptions for a medication that has not been proven to be safe or effective. Congress, the federal government, and the individual states never intended to make such payments and would have never made such payments but for the conduct of Parke-Davis. Although Parke-Davis did not submit the claims and did not directly receive Medicaid payments from the states and the United States, Parke-Davis has been the greatest beneficiary from this pattern of unlawful conduct, filling thousands of prescriptions for Neurontin which would have never been placed but for its unlawful conduct.

WHEREFORE, the Plaintiff demands judgment on behalf of the United States, together with all costs, fees, awards, and interests permitted by 31 U.S.C. § 3730 as a result of each and every false claim caused by Parke-Davis.

PLAINTIFF DEMANDS A TRIAL BY JURY ON ALL CLAIMS.

**DAVID FRANKLIN, on behalf of
THE UNITED STATES OF AMERICA**

By His Attomeys,

**Thomas M. Greene, Esq., BBO # 210020
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Food and Drug Administration's Request for Comment on First
Amendment Issues